April 27, 2000

VETERINARY SERVICES MEMORANDUM NO. 800.51

Subject: Additives in Animal Biological Products

To: Biologics Licensees, Permittees, and Applicants
Directors, Center for Veterinary Biologics

I. PURPOSE

This memorandum clarifies policies and procedures to comply with the requirements of 9 CFR l03.2(b) and (c), l03.3(f) and (g), and 112.2(a)(8) concerning slaughter withholding periods for animals used for food purposes that have been treated with biological products formulated with additives.

II. CANCELLATION

This memorandum cancels Veterinary Services Memorandum No. 800.51, dated October 22, 1984.

III. BACKGROUND

A. Additives

Additives in veterinary biologicals may consist of adjuvants, carriers, inactivating agents, preservatives, or other substances or ingredients that are added to cultures of microorganisms in the formulation of biological products that are used to treat animals. The regulations in 9 CFR 103.3(f) specify that firms using such additives must submit data demonstrating that use of the product does not result in the presence of any unwholesome condition in the edible parts of animals presented for slaughter.

B. Authority and Consultation

The regulations in 9 CFR 112.2(a)(8) prescribe a withholding period of not less than 21 days for animals that may be used for food purposes that have been treated with veterinary biological products containing additives. The Administrator may prescribe a longer withholding period on the advice of the Food Safety Inspection Service (FSIS) which advises the CVB-LPD regarding the use of additives in products used to treat animals.

IV. **POLICY**

A. Ingredients of Animal Origin

Each lot of ingredient additive of animal origin used to prepare a biological product must be heat sterilized, or tested as prescribed in 9 CFR 113.53.

B. Ingredients Not of Animal Origin

Ingredients or other substances used in biological products that are not of animal origin must meet acceptable standards for purity and quality as specified in 9 CFR 113.50 and the filed Outline of Production.

C. Specific Food Safety Clearance Requirements

1. Clearance must be obtained for products that contain additives that are used as adjuvants.

2. Clearance must be obtained for products that contain new formulations of previously approved additives that are significantly different from those previously approved.

3. Clearance must be obtained for each species for which the product containing an additive is recommended.

4. Clearance must be obtained for each method or route of administration for which a product containing an additive is recommended.

V. **CLEARANCE PROCEDURES**

A. Describe the Additive

Specifications for each additive such as source, grade, and quality of chemical additives and/or treatment and testing performed on each lot of ingredients of animal origin must be described in the filed Outline of Production.

B. Supporting Data

In order to determine an appropriate withholding period, applicants should be prepared to submit to CVB the following information:

1. The results of toxicological studies to determine local and/or systemic effects of the additive on laboratory animals. The results may either be from studies performed by the applicant or taken from the material safety data sheets obtained from the supplier of the additive.

2. The results of gross and/or microscopic examination of the injection site(s) of host animals treated with experimental product that contains the additive, and

3. Data showing the time required for the resolution of any injection site reactions.

C. Food Safety Form

CVB-LPD will prepare and transmit the supporting data to the FSIS requesting food safety clearance of the product and a recommendation regarding the appropriate withholding period. The FSIS will:

1. Specify a minimum withholding period, or

2. Specify additional data, or

3. Recommend the postmortem inspection of a specified number of experimental animals at slaughter for food use purposes. Applications for permits to slaughter animals treated with experimental products may be obtained from:

Residue and Pathology Correlation Branch
USDA - FSIS
Technical Service Center
1299 Farnam St., Suite 300, Landmark Center
Omaha, NE 68102

/s/

Alfonso Torres
Deputy Administrator
Veterinary Services